Award Number: W81XWH-09-2-0184

TITLE: Near-infrared spectroscopy to reduce prophylactic fasciotomies for and missed cases of acute compartment syndrome in soldiers injured in OEF/OIF

PRINCIPAL INVESTIGATOR: LTC Brett Freedman, M.D.

CONTRACTING ORGANIZATION: The Geneva Foundation

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14. ABSTRACT
The research project is a three-part project to validate the accuracy and reliability of a specific NIRS sensor (Equanox, Nonin, Inc, Plymouth, MN) in diagnosing acute compartment syndrome in injured combat soldiers. Part 1 is a series of two observational studies, the first of which was completed at Landstuhl Regional Medical Center during year 1. The second clinical study was originally planned to be conducted in theatre in Afghanistan and Iraq, but had to be transitioned to a FDA-regulated study conducted under an abbreviated IDE within the USA. In the current reporting period this study was implemented at three trauma centers in Georgia. The study is well underway with 44% of the subjects required by the protocol enrolled. We are on track for completing the study within the third quarter of the extended fourth year. Part 2 of the project involves animal studies to address issues raised in clinical testing and furthering understanding of NIRS response to ACS. The first animal study was completed in Year 2 of this award, and a second study using a different ACS model was completed in the current reporting period. Part 3 of this project is the translation of the current technology into a validated, FDA approved format. Data collected in Parts 1 and 2 will be used as the basis for developing a NIRS-based diagnostic algorithm that will be validated in a subsequent clinical trial.

15. SUBJECT TERMS
Near Infra-Red Spectroscopy, acute compartment syndrome

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INTRODUCTION

This research study is a three-part project planned to be conducted over three years to validate the accuracy and reliability of using Near Infrared Spectroscopy (NIRS) to diagnose acute compartment syndrome (ACS) in combat soldiers and civilians sufferring high energy trauma to the lower extremities. Part 1 was to be two clinical observational studies. The first part (Phase I) was conducted at Landstuhl Regional Medical Center and was started in the first year of this award and completed on budget. The second study (Phase 2) was originally planned to be conducted in theater at Level III CSHs in Afghanistan and Iraq with support from the Joint Combat Casualty Research Team (JC2RT) and a researcher who specifically deployed to lead this study in-theater. However, during the protocol review process, USAMRMC petitioned for a pre-IDE determination from the FDA, and it was decided that the study needed to be conducted as an FDA-regulated study (with "abbreviated requirements"), and was transitioned to three civilian hospitals in the state of Georgia. This transition caused over 12 months delay in initiating the study, as described in our previous annual report. Because of this delay, we are seeking an extension for this award into a fourth year and if awarded, we will be on track for completing enrollment in the Phase 2 study by the third quarter of this fourth year, which will mark successful completion of all original tasks for this grants Statement of Work.

Part 2 (Task 3) of this award uses porcine models of ACS to further evaluate and validate the clinical utility of using continuous NIRS monitoring to diagnose ACS. The initial experiments using albumin infusion and contusion/albumin infusions models for inducing ACS were successfully completed on target by the end of the second year of this grant. These studies demonstrated that NIRS measurement of hemoglobin oxygen saturation in the tibial compartment provided reliable and sensitive correlation to increases and decreases in intra-compartment pressure and intra-compartment perfusion pressure. This year we have built on the success of the animal experiments by employing a second model of tibial compartment syndrome which uses an inflatable balloon to increase intra-compartment pressure.

The final part of this project (Tasks 4–6) will include the translation of the current technology into a proven means for detecting the presence of critical hypoperfusion of the leg compartments indicative of acute compartment syndrome. The data collected in our Phase 1 and 2 clinical studies and the animal studies will be used to develop a diagnostic algorithm, and ultimately form the basis for a subsequent clinical trial to validate this algorithm and lead to the first FDA indicated diagnostic device for ACS. The current FDA approved indication for the NIRS device used in our clinical studies (the Nonin Equanox ^{TM} 7600 oximeter) is for monitoring regional tissue oxygenation. This device has been validated and is currently marketed as a means for detecting altered states of perfusion in normal (i.e. not traumatically injured, specifically cerebral) tissue. Our research is pushing this technology to its limits, by seeking to monitor altered perfusion states in abnormal (i.e. traumatically injured) tissue. In this Period and Period 4, our industry partner and this research team have sought and will continue to identify areas to improve this technology in the reduction to practice of a ACS diagnostic device. The FDA indication we will seek to develop, submit and defend using the results of the clinical and animal studies conducted under this grant and the subsequently planned clinical study is a diagnostic indication such that the device can be approved to provide information that directly impacts clinical decision making. This function will meet the critical unmet need in combat casualty care originally identified in our grant proposal.

BODY

The primary goal of work conducted in Period 3 was to establish the Phase 2 clinical study at three sites in the state of Georgia, and to start subject enrollment. This has been accomplished and we are on target to complete subject enrollment within the first three quarters of the potentially extended Period 4.

TASK 1: Human Use Study – Phase 1

1a – g: All tasks completed on time and within budget in Periods 1 and 2

TASK 2: Human Use Study – Phase 2

2a – c: Tasks completed in Period 2

2d: Conduct Phase 2 Prospective Observational Study

As discussed in our previous annual report, this study was originally planned to be conducted in theater in Afghanistan and Iraq, but due to decisions by the USAMRMC and FDA, the study had to be transitioned to the civilian setting. This caused a 12+ month setback in our timeline, but we are seeking a one year extension, and a budget increase to provide for this transition and completion of this study in the civilian setting.

At the end of the previous period, three sites had been selected in Georgia – Grady Memorial Hospital (GMH), Atlanta Medical Center (AMC) and Athens Regional Medical Center (ARMC). During the current Period we have successfully established research teams covering all the sites, implemented study-related procedures, data collection and management procedures, trained the research teams, obtained IRB and HRPO approval to conduct the study at these sites, trained the hospital staff at each center on the study, established and implemented an FDA-compliant medical monitoring program and begun enrolling subjects. Issues and setbacks were encountered along the way but solutions were implemented as described in this annual report and this Period's quarterly reports, and we are still on track for a successful completion of this study before the end of the third quarter of Period 4. Major milestones achieved for each site are outlined in Table 1.

Site	Initial IRB Approval	Initial HRPO Approval	Start of Patient Screening	First Subject Enrolled
GMH	12/20/2011	01/13/2012	03/23/2012	03/26/2012
AMC	11/10/2011	04/11/2012	08/10/2012	08/30/2012
ARMC	12/29/2011	05/17/2012	08/01/2012	08/20/2012

Table 1: Major Milestones in the establishment and initiation of clinical research sites for the NIRS study

Screening and Enrollment – Cohort 1

Cohort 1 subjects serve as control subjects that are critically injured, but do not have any lower extremity injuries. They are being recruited only at GMH. Screening for Cohort 1 began in June, 2012 (third quarter of Year 3). Patients are screened for inclusion into Cohort 1 by a daily review of all trauma admissions to the ICU. Patients that meet most eligibility criteria are then followed up on to complete screening, determine eligibility and request consent from the patient or from a legally authorized representative if the patient is not capable of providing consent on their own behalf. To date, 379 patients admitted to the ICU with trauma have been screened (Figure 1) and 19 have been enrolled out of a total cohort requirement of 25 subjects (Table 2). However, five of these subjects were withdrawn before NIRS monitoring commenced because they were subsequently deemed ineligible, or consent was withdrawn. Additionally, two subjects withdrew consent after two or four hours of monitoring. Consequently, an extended period of NIRS monitoring has been captured for 12 Cohort 1 subjects. In the next Period we will extend the Cohort 1 size by 7 additional patients, to insure we have complete data sets for a total number of 25 subjects in this cohort.

As illustrated in Figure 1, the most frequent reason potential Cohort 1 patients were excluded accounting for 38.3% of all patients screened (145 of 379 patients) was because their expected length of stay was less than

48 hours. Most of these patients were admitted to the ICU for observation following a concussion, or were not critically injured. A few were very critically injured and were not expected to survive. The age of the patient not falling within the 18 to 65 year range was the next most frequent reason for exclusion (65 patients, 17.2%) or that they had bony or vascular injuries to their lower extremities (44 patients, 14.5%). Forty-two patients were excluded for reasons not outlined in the eligibility criteria, but they were considered unsuitable research candidates. The majority of these patients were combative or uncooperative to their medical care, or they had significant psychological problems or severe comorbidities.

All ICU Admissions for Trauma	Number	Percentage
Expected length of stay < 48 hours	145	38.3
Age not in 18 to 65 range	65	17.2
Bony or vascular injury to lower extremity	55	14.5
Other reason	42	11.1
ENROLLED	19	5.0
Declined consent	14	3.7
In police custody	12	3.2
No LAR to provide consent	11	2.9
Spinal cord injuries causing paralysis	5	1.3
Application of sensors would impede care	4	1.1
No uninjured upper extremity	3	0.8
Is potentially pregnant	2	0.5
Admission not trauma-related	2	0.5
TOTAL	379	100

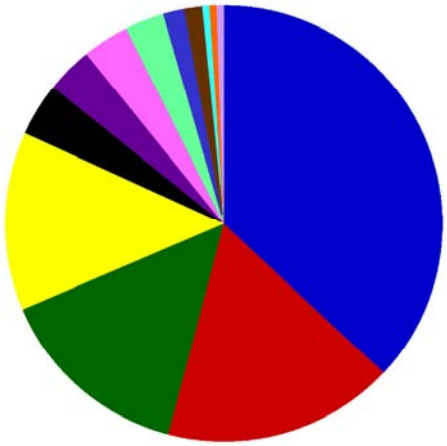

Figure 1: Screening breakdown for potential Cohort 1 inclusion to date

Screening and Enrollment – Cohorts 2 and 3

Cohort 2 subjects are patients with tibia/fibula shaft or tibial plateau fractures that are caused by high energy impacts and are therefore likely to develop ACS. All patients admitted to participating hospitals with tibia fractures are screened for inclusion. Coordinators are notified by the treating resident of all admissions potentially meeting eligibility criteria, and the coordinators do the detailed screening. Cohort 3 (previously called Cohort 2C) subjects are Cohort 2 subject s that subsequently are clinically diagnosed with ACS, receive surgical fasciotomies to treat the ACS, and move from Cohort 2 to Cohort 3.

All Patients with Tibia/Fibular Fractures	Number	Percentage
ENROLLED	34	35.8
Did not meet injury severity criteria	18	18.9
Outside 12 hour enrollment window	12	12.6
Declined consent	8	8.4
Outside 18 to 65 age range	8	8.4
Vascular injury to leg	6	6.3
No uninjured upper extremity	2	2.1
No LAR to provide consent	2	2.1
Other reason	2	2.1
Fasciotomy prior to enrollment	2	2.1
Prior injury to leg that might alter circulation	1	1.1
TOTAL	95	100

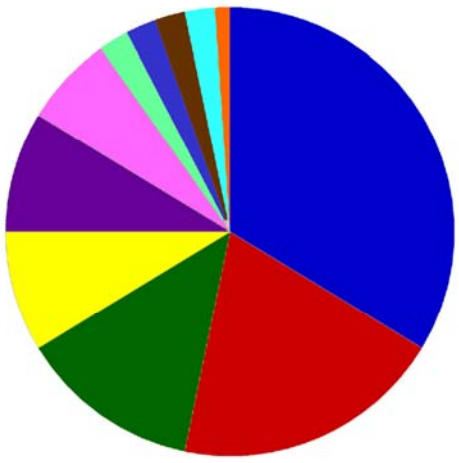

Figure 2: Screening breakdown for potential Cohort 2 inclusion to date.

Screening for Cohort 2 began in March 2012 at GMH, but was placed on hold through April and May for further refinement of procedures and training of coordinators and hospital staff. Screening began at AMC and ARMC in August. By the end of the current Period 3, 95 patients with tibia fractures had been screened (Figure 2) and 31 subjects had been enrolled (Table 2) out of the 95 required by the protocol. Of these only one patient

developed ACS and moved into Cohort 3. The most frequent reasons for patients to fail screning was that their fractures did not meet the severity criteria set forth in the protocol (18 patients, 19.6%) or they could not be consented and enrolled within 12 hours of their injuries (12 patients, 13.%). The issue of required informed consent for this no greater than minimal risk protocol, using a nonsignificant risk medical device, has been a known significant problem, and was the core issue related to the transition of Phase 2 from a military combat setting to the civilian trauma centers. This is a problem that is outside our control, yet we have sought all options to mitigate its impact. For example, most of the latter patients were identified earlier in the recruitment process and the coordinators were not notified of the patient immediately. Further training of the providers and research team has greatly reduced the number of potential patients lost.

GMH		AMC	ARMC	Total	Required By Protocol	Percent Completed
Cohort 1	19	N/A	N/A	19	25	76.0%
Cohort 2	23	5	5	33	95	35.8%
Cohort 3	1			1		
TOTAL 43		5	5	53	120	44.2%

Table 2: Number of Cohort 1, 2, and 3 subjects enrolled in the study across all three participating sites

Enrollment Summary

As illustrated in Table 2, we have enrolled a total of 53 patients into Cohorts 1, 2, and 3. This represents 44.2% of the total number of subjects required by the protocol, 76% of the Cohort 1 requirement (19 out of 25) and 35.8% of the Cohort 2 requirement (34 out of 95). Cohort 1 will be complete soon. The majority of the Cohort 2 subjects (30 subjects) were recruited in the months of June, July, August, and September, although only GMH was recruiting in June and July. This represents an enrollment average of about 7.5 Cohort 2 subjects per month. At this rate we will complete enrollment for this study on target within the next eight months (third quarter of year 4).

2e: Analyze Data, Provider Feedback

Not due until completion of the Phase 2 study, planned for the second half of Year 4.

2f: Present and Publish Results of Phase 2 Study

Not due until completion of the Phase 2 study, planned for the second half of Year 4.

TASK 3: Animal Use Study – First Porcine Study

3a – e: The first study in a series of 3 ACS injury models was completed within Period 2, and successfully demonstrated a correlation between NIRS values and intra-compartment perfusion pressure (TIPP) in a tibial fracture model.

3f: Present and Publish Pig Study Findings

During the year, abstracts summarizing the results of the first pig study were submitted to

- The 125th Annual Meeting of the American Orthopedic Association – poster presentation in June,
- The 2012 Orthopedic Trauma Association Annual Meeting – podium presentation in June,
- The 2012 Military Health System Research Symposium – presented in August
- The 2013 American Academy of Orthopaedic Surgeons Meeting (awaiting acceptance)

A manuscript was also prepared and was submitted to The Journal of Orthopedic Trauma. Copies of these abstracts and manuscript are included in this Annual Report as Appendix A.

TASK 3: Animal Use Study – Second Porcine Study

After successful completion of the albumin infusion and contusion/albumin infusion models, a third porcine model was developed and implemented, based on work from the US Army Institute of Surgical Research. The new model is a tibial compartment syndrome model that produces consistent intra-compartmental muscle swelling, microvascular compromise and tissue hypoperfusion as well as predictable extensive tissue damage. The injury model is created by inserting a balloon catheter between the anterior muscle compartment and the anterior face of the tibia. This is a reperfusion model of ACS. Baseline NIRS values and tibial intra-compartmental pressure (TICP) are measured then a compartment syndrome injury is created by inflating the balloon catheter with saline to sustain TICP at 30 mmHg above mean arterial pressure which is sustained for 6 hours. After 6 hours, the balloon is deflated, allowing for reperfusion of the compartment. Tissue oxygenation was monitored continuously using NIRS, and TICP was assessed for the duration of the 6 hour induction of compartment syndrome and the 8 hour reperfusion and recovery period. This study is also contracted to the University of Georgia (UGA) College of Veterinary Medicine and is being completed under a no-cost extension.

3a: Created UGA IACUC Protocol Application for Animal Studies
During the current year, the protocol for the reperfusion porcine study was developed and submitted to the UGA IACUC.

3b: Obtain UGA IACUC and USAMRMC ACURO Approvals for Second Study
The UGA IACUC approved the protocol on 02/08/2012. It was submitted to the USAMRMC ACURO and received their approval on 02/24/2012.

3c and d: Initiate and Conduct Animal Studies
The reperfusion pig study was conducted and completed on time in the third quarter of this performance year. Nine animals were used in the study, seven of which produced usable data to be included in the final analysis. The results of the experiment indicated that while intra-compartmental pressure increases with muscle damage, there is not a complete loss of tissue oxygen saturation in the tissue over the 14 hours of the protocol.

In the final quarter of Period 3 we began planning the last of the animal studies, in which we plan to evaluate the NIRS response to a "missed" compartment syndrome. This model will use NIRS to monitor the changes that take place when a fasciotomy is performed too late and muscle has died. This study will be initiated in the 1st quarter of the 4th period under a no-cost extension at UGA, if awarded.

3e and f: Analyze Data and Prepare for Presentation and Publication
This work is underway at the end of this performance period and will be continued into the fourth year.

TASK 4: Reduction to Practice and FDA Approval Process

4a: Finalize product development relationships between Nonin, Inc and J+M Shuler – Completed in Year 2

4b: Begin reduction to practice process – Ongoing

4c: Produce final prototype for use in completion of Phase 1, all of Phase 2 and the investigational clinical study to be supported by a future grant. Ongoing -The current embodiment, more specifically the spectroscopy technology is mature and ideal for our intended indication. In this light, we feel we have a final prototype. There are still planned small physical improvements, for example, increasing the number of ports per machine, but these improvements will not affect the results of our planned studies.

4d: Respond to provider feedback re: functionality and industrial design - Completed. In our experience with the device, the only two significant physical improvements needed are the addition of more ports to a single machine, so that a single patient can be monitored by a single machine, and "horse-tailing" of leads, such that 4 sensors connect to a single cable about 1 foot or less from the patients leg and that cable then runs back to the device, to cut down on cable clutter in the current system. Both of these changes are small and will not affect our results. To get broader feedback, we have included provider feedback into the CRF for the Phase 2 study. The primary product development piece to occur over the course of this grant and in work to follow the conclusion of this grant will be the development and then validation of a diagnostic algorithm, for which a new FDA indication will be applied that approves the use of this device as a diagnostic tool for acute compartment syndrome.

TASK 5: Coordination between study sites

5a: Bi-annual collaborators meeting – Ongoing. Given the transition from LRMC as a research site for the Phase 2 clinical study, to the Atlanta area, we have increased on-site visits to 3/year. On site visits during Period 3 include:

- 16 to 17 February 2012 – Site training and initiation
- 19 to 20 April 2012 – Site retraining and re-initiation
- 02 to 03 August – Final review with AMC IRB, evaluation of current status

5b: Conduct weekly VTC (Telcon) for LRMC/J+M Shuler, and OIF/OEF during Phase 2 – No longer required since Phase 2 study is not being conducted in Georgia and not at LRMC.

5c: Rapid interpretation of weakness in the design and function of sequential NIRS pad prototypes and NIRS monitoring algorithms. – Ongoing. The device is in a state where it is and has been fully ready for testing in our studies. It will probably undergo some minor physical improvements with time. The major improvement will be the design and validation of a diagnostic algorithm based on NIRS values. This process is ongoing and will continue past our grant period. This process will ultimately require validation in a prospective interventional trial.

5d: Coordinate response to FDA requests for information during approval process : Ongoing. LTC David Shoemaker, Marieann Brill and "Decision Gate" are all involved in USAMMDA's sponsorship of this project and the creation/maintenance of a FDA compliant medical monitoring program for the 3 clinical sites in Phase 2. As a result, this Phase 2 study will be permissible for inclusion in the "burden of proof" submission for our ultimately new FDA 510k approved indication.

5e: Insure mandatory reporting to SAMMC, ISR & USAMRMC is maintained: Ongoing and in good standing.

TASK 6. Future Research Endeavors

At the completion of Tasks 1-5 we will have a publically available, FDA-approved monitoring device with solid basic science and initial clinical research support. The main outcome of this task is to start the next step, which is the creation and validation of NIRS-base clinical guidelines for the diagnosis and treatment of acute compartment syndrome to support a new FDA indication for the Nonin Equinox™ as a DIAGNOSTIC device, on top of its currently approved monitoring indication. This task requires clinical investigational trials that will follow the conclusion of this grant.

PROBLEM AREAS

Sensors not picking up signal on some injured legs

Issue: We have discovered that on certain subjects the sensors on the injured leg are unable to pick up or maintain a signal that is usable by the Nonin 7600 Monitor. Our current belief is that this is because the amount of light reflected back to the sensors or the calculated percent oxygenation fall outside certain thresholds. Based on prior indications for the device, the monitor's analysis algorithm interprets this as a problem in the system such as the sensor becoming detached from the pod, or loss of integrity in the application of the sensor to the patient. An error message is generated and an oxygenation value is not displayed or recorded. The error messages can be mechanical (i.e. the sensor wire disengages from the pod) and when they are, they can be resolved by checking the sensor's connection to the pod and patient, sometimes necessitating replacing the sensor. However, we have encountered cases where regular troubleshooting of the system according to Nonin procedures and including replacement of sensors has not rectified the problem. A usable signal cannot be obtained in these cases.

Resolution: We have been working diligently with Nonin to resolve this issue. Just prior to the close of this reporting period Nonin had presented a solution where a different monitor – the 7610, could be used to capture individual raw wavelength data, a robust amount of information that is not displayed or recorded by the 7600 oximeter. The 7610 oximeter uses the same sensors (i.e. patient interface) as the 7600, but it records all light data in its raw state, to allow for thorough investigation of the source of error messages, that do not resolve with troubleshooting measures aimed at mechanical problems. It is a USB connection into a laptop running the Nonin data collection software, rather than into a dedicated monitor. All 12 sensors will remain in place on the subject. The sensor(s) that is generating the error will be plugged into the 7610 oximeter while the others will remain connected to the 7600 oximeter. This setup will temporarily replace the trunk cable and 7600 monitor display and will allow the oximetry pods to capture additional wavelength data which is stored on the laptop. This process needs to only collect 1-2 minutes of data. Then the patient is reattached to the standard 7600 set-up.

Using the 7610 will have no effect on the subject's participation in the study since it uses the same sensors as the 7600 model. The sensors do not need to be replaced. The only difference between the two monitors is that the 7610 model captures raw wavelength data, while the 7600 model does not. Collecting wavelength data using the 7610 monitor will allow greater detail of information and flexibility in the analysis of tissue oxygenation levels.

Although the 7610 oximeter has not been cleared by the FDA, its intended use, indications for use, and the associated risks of the monitor are consistent with those associated with the 7600 model, which is being studied as an investigational device under this protocol. Both are integrated, digital devices for measuring regional hemoglobin oxygen saturation of blood underneath the sensor. They are used to monitor critical organ health, specifically of the cerebral cortex, allowing early intervention to prevent ischemia.

Progress: At the end of the reporting period, a protocol amendment had been prepared to include the use of the 7610 oximeter, and this had been submitted to our USAMMDA regulatory personnel for review ahead of submitting the amendment to the respective IRBs. Nonin had modified the 7610 device and laptop such that it could be used in the study. They will be bringing the device to Atlanta and will train the coordinators on its use in mid October. The regulatory approvals allowing use of this device should be in place by the middle of November. Further, we have already added locking mechanisms to the pods, that prevent the most common mechanical error, which is the sensor disengaging from the pods.

KEY RESEARCH ACCOMPLISHMENTS

1. Established the Phase 2 clinical study protocol at three sites in the State of Georgia, set up study procedures and trained coordinators.

2. Recruited 44.2% of subjects required by the protocol (53 out of 120) and on track for completion of subject enrollment during the third quarter of year 4.
    - Cohort 1 – 76.0% completed (19 out of 25 subjects)
    - Cohorts 2 and 3 – 35.8% completed (34 out of 95 subjects)

3. Four abstracts prepared, submitted, and presented covering the results of the first pig study.

4. One paper published, and another manuscript prepared.

5. Reperfusion pig study developed, approved through UGA IACUC and USAMRMC ACURO, initiated and completed.

REPORTABLE OUTCOMES

Accepted/Presented Abstracts

Freedman B (2012) NIRS versus direct pressure monitoring of acute compartment syndrome in a porcine model. Military Health Systems Research Symposium.

Cathcart C, Shuler M, Freedman B, Reynolds L, Cole A, Budsberg S, Whitesides T and Smith E (2012) Non-invasive NIRS versus invasive direct pressure monitoring of acute compartment syndrome in a porcine model. American Orthopedic Association Meeting.

Cathcart C, Shuler M, Freedman B, Reynolds L, Cole A, Budsberg S, Whitesides T NIRS vs direct pressure monitoring of acute compartmental syndrome in a porcine model.

Cathcart C, Shuler M, Freedman B, Reynolds L, Cole A, Budsberg S, Whitesides T (2012) NIRS versus direct pressure monitoring of acute compartmental syndrome in a porcine model. Orthopedic Trauma Association Meeting.

Published Papers

Cole A L, Herman R a, Heimlich J B, Ahsan S, Freedman B A and Shuler M A (2012): Ability of Near Infrared Spectroscopy to Measure Oxygenation in Isolated Upper Extremity Muscle Compartments. Journal of Hand Surgery 37A: 297 – 302.

Manuscripts Submitted

Curtis C. Cathcart, DVM, Michael S. Shuler, MD, Brett A. Freedman, MD, Lisa R. Reno, BS, Ashley L. Coles, MPH, Steven C. Budsberg DVM, MS Correlation of near infrared spectroscopy (NIRS) and direct pressure monitoring in an acute porcine compartmental syndrome model. Journal of Orthopaedic Trauma (Submitted)

CONCLUSIONS

Significant progress has been made during the third year of this award and we are on course for completing our commitments on time by the end of the upcoming fourth year. The Phase 2 clinical study, originally planned to be conducted in Afghanistan and Iraq, was successfully transitioned to an FDA-regulated study to be conducted at three civilian trauma centers in the state of Georgia – Grady Memorial Hospital, Atlanta Medical Center and Athens Regional Medical Center. During the year we received approvals to conduct the study at these sites from the respective local IRBs and from the USAMRMC's Human Protections Office. Research teams were established and trained, and patient screening and subject enrollment commenced. At the end of the reporting period we had enrolled 44.2% of the subjects required by the protocol.

Data from the initial animal studies that were completed in the previous year was analyzed and presented at four conferences. A manuscript has also been prepared. Based on the successful outcome of that study, an additional study was designed using a different model of porcine compartment syndrome. During this year, the protocol was prepared and received approval from the UGA IACUC and the USAMRMC ACURO. The study was initiated and completed. Nine animals were used in the study and usable data was captured from seven animals. We have one final study planned, for the 4th period and are currently seeking an extension for this period.

We have had to overcome many unforeseen hurdles in the execution of this award, most particularly in relation to the USAMRMC's decision that this study needed to be conducted as an FDA-regulated study which required its transition from the military theater in Afghanistan and Iraq to the civilian setting in the USA. This transition consumed 12 months of valuable performance time, which necessitated a one year extension of the performance period. We have worked diligently over the last year to ensure that the study was established in Georgia according to FDA requirements such that the data can be used to support an FDA regulatory submission. The study is now well underway and we expect to have subject enrollment completed within the third quarter of the upcoming fourth year of this award.

REFERENCES

None.

Appendix 1 – Presented Abstracts

Abstracts - Accepted

1. Military Health Systems Research Symposium (2012)
2. American Orthopedic Association (2012)
3. Orthopedic Trauma Association (2012)

Abstracts – Submitted

1. American Academy of Orthopedic Surgeons (2013)

Published Manuscripts

1. Cole AL, Herman RA, Heimlich JB , Ahsan S, Freedman BA and Shuler MS (2012): Ability of Near Infrared Spectroscopy to Measure Oxygenation in Isolated Upper Extremity Muscle Compartments . Journal of Hand Surgery 37A: 297 – 302.

Prepared Manuscripts – Not Yet Accepted for Publication

1. Cathcart CC, Shuler MS, Freed man BA, Reno LR and Budsberg SC: Correlation of Ne ar Infrared Spectroscopy (NI RS) an d Direct Pre ssure Monitoring in an Acute Porcine Compart mental Syn drome Model.

NIRS VERSUS DIRECT PRESSURE MONITORING OF ACUTE COMPARTMENTAL SYNDROME IN A PORCINE MODEL

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PURPOSE: Assess the correlation of near infrared spectroscopy (NIRS) and tibial intra-compartmental perfusion pressure (TIPP) in a porcine model of acute compartment syndrome (ACS). **DESIGN:** Animal research **POPULATION STUDIED:** 31 Landrace swine (16 control; 15 acute trauma). **METHOD:** Pigs were positioned in dorsal recumbency, and maintained on isoflurane with positive pressure ventilation. A median saphenous artery was catheterized for direct arterial pressure measurement. On each tibia, a NIRS sensor (Nonin, Plymouth, MN) was centered over the craniolateral muscle compartment. On the test leg, two 18-gauge needles were centered on each side of the sensor for direct pressure transducer measurement of TICP. For infusions, 5% albumin was infused through 2 18-gauge needles to elevate tibial intra-compartmental pressures (TICP). A single 18-gauge needle lateral to the midpoint of the NIRS sensor on the control leg monitored TICP. Continual time synchronized blood pressure (BP) measures of systolic (SAP), diastolic (DAP), and mean pressures (MAP), pulse rate (HR), respiratory rate (RR), systemic pulse oximetry (pulse ox), body temperature (T), TICP, and NIRS from each leg were measured. For the control group (N=16), transducers were zeroed and TIPP ([=DBP – TICP]) of the test leg was incrementally increased by albumin infusion. Continuous measurements (NIRS, BP, HR, RR, pulse ox, T) were taken at baseline for 10 min, and then for 5 min each at TIPP=40, =30, =20, and =10 mmHg, and then 10 min each at TIPP=0 mmHg, =MAP, =SAP and =SAP+10 mmHg. Fasciotomies were then performed bilaterally and measurements were recorded for 10 min. For the trauma group (N=15), baseline measurements were obtained for 10 min after which sensor and needle placement was marked and then removed from the test leg. The limb was stabilized and trauma induced by dropping a 2 kg weight 30 times down a 100 cm cylindrical tube over the craniolateral aspect of the limb. Instrumentation was replaced, a 45 min equilibration period observed, and infusion protocol performed as described above. **DATA ANALYSIS:** For each group, repeated measures ANOVA tested for differences in TICP, TIPP and NIRS. Tests were 2-sided with $\alpha<0.05$ considered significant. Pearson's correlations were calculated between TICP and NIRS, and TIPP and NIRS. **FINDINGS:** TICP was significantly higher for the test versus control limb at all time-points except TIPP=40 mmHg and >5 min following fasciotomy. NIRS detected significant changes in tissue oxygenation at all time points in which TICP was significantly elevated. Once TIPP reached 20mmHg, NIRS decreased significantly from baseline and did not return to baseline levels until >5 min after fasciotomy. NIRS detected decreased oxygenation at each interval of TIPP decrease and a subsequent increase following fasciotomies. Significant negative correlations of TICP and NIRS and positive correlations of TIPP and NIRS were observed. **CONCLUSIONS:** NIRS provided a reliable, sensitive measure correlating to both an increase and decrease in TICP and TIPP, respectively in this model; acute trauma did not alter the strength of correlation between NIRS values and TICP or TIPP. **IMPLICATIONS:** Further research is needed to determine at what NIRS reading a fasciotomy may be indicated to prevent permanent tissue damage. **FROM/TO TIME PERIOD:** Data collected February through May 2011. **FUNDING:** This study was funded by the Department of Defense Deployment Related Medical Research Program (DRMRP) #DR080018.

Non-invasive NIRS versus invasive direct pressure monitoring of acute compartment syndrome in a porcine model

Curtis Cathcart, Michael Shuler, Brett Freedman, Lisa Reynolds, Ashley Cole, Steven Budsberg, Thomas Whitesides, Emily Smith

SUMMARY:
This study aimed to correlate near infrared spectroscopy (NIRS) values and the tibial intra-compartmental perfusion pressure (TIPP).Compartment pressures were manually elevated and continually monitored using NIRS. This study provides data that establishes a correlation between NIRS measurement of hemoglobin oxygen saturation and TIPP.

OBJECTIVE:
Near Infrared Spectroscopy (NIRS) has been proposed to provide continual, real time, non-invasive monitoring of traumatized extremities. The aim of this study was to correlate NIRS values and tibial intra-compartmental perfusion pressure (TIPP) in a porcine model of acute compartment syndrome.

METHODS:
In 16 swine, TIPP of the test leg was increased incrementally by albumin infusion and measured at pre-determined intervals. Continual, time synchronized measurements of systemic blood pressure – systolic (SAP), diastolic (DAP), and mean pressures (MAP), pulse rate, respiratory rate, systemic pulse oximetry, body temperature, compartmental pressures (2 transducers on test leg and one on control leg), and regional oximetry from the NIRS sensors from each leg were collected. Fasciotomies were performed once tibial intra-compartmental pressure (TICP) exceeded SAP. A repeated measures model was used to test for differences in TICP, TIPP and NIRS values between test and control legs and time points. Multiple comparisons were adjusted for using Tukey's test. All tests were 2-sided with $\alpha = 0.05$. Pearson's correlations were calculated between TICP and NIRS and between TIPP and NIRS.

RESULTS:
The model successfully created consistent, reproducible increases in TICP and decreases in TIPP. Significant increases in TICP between test and control limbs at all time points with the exception of TIPP of 40 mHg and at 5 and 10 minutes following fasciotomies were found (Figure 1). Concurrently, NIRS was able to detect significant changes in tissue perfusion at all time points. There was a significant negative correlation of TICP and NIRS measurements ($r=-0.79$, $p<0.0001$). NIRS was able to detect increased tissue oxygenation following pressure relieving fasciotomy.

CONCLUSION:
NIRS of the compartment provided a reliable, sensitive measure correlating to both an increase in TICP and a decrease in TIPP in this porcine tibial model. Additionally, a release in pressure through fasciotomy resulted in a predictable return to normal NIRS values.

Figure 1.

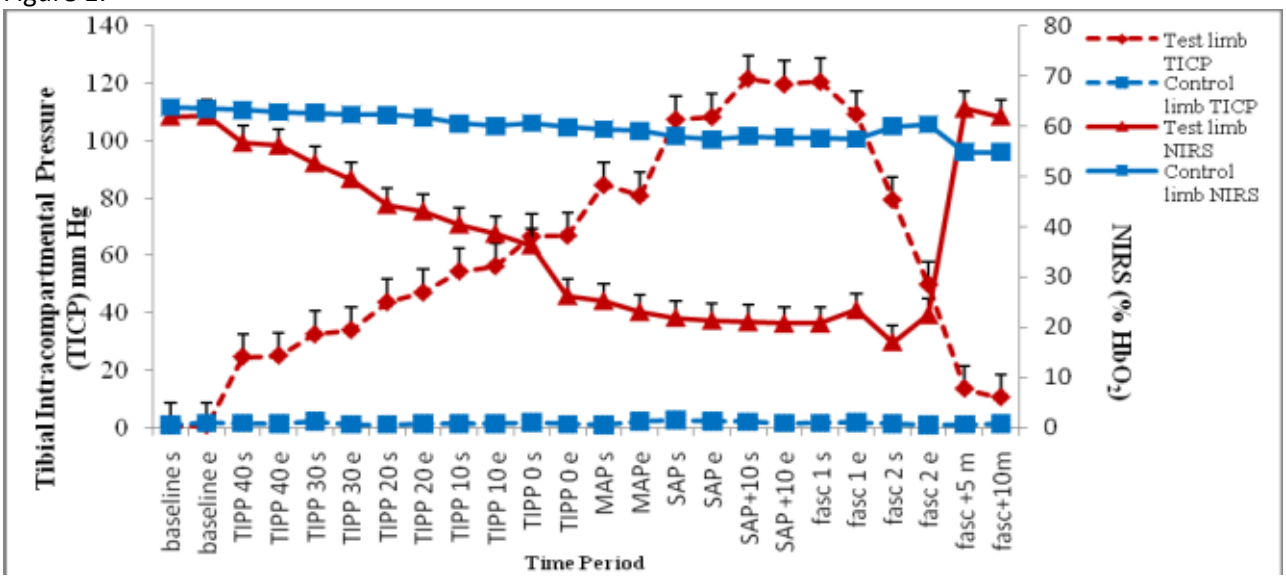

Figure legend:
s: start of each period, e: end of each period
MAP: TIPP = mean arterial blood pressure
SAP: TIPP = systolic blood pressure
SAP+10: TIPP = systolic blood pressure + 10 mm Hg
fasc 1: caudolateral fasciotomy, fasc 2: craniolateral fasciotomy

NIRS vs Direct Pressure Monitoring of Acute Compartmental Syndrome in a Porcine Model

Purpose: Acute compartment syndrome (ACS) can have devastating sequelae if missed or if treatment is delayed. Near infrared spectroscopy (NIRS) has been proposed for continual, non-invasive monitoring of traumatized extremities. This study sought to correlate NIRS and the tibial intra-compartmental perfusion pressure (TIPP) in a porcine model of ACS. **Methods:** The study consisted of Landrace swine divided into two groups: control (N=16) and acute trauma (N=15). All pigs were maintained on isoflurane with positive pressure ventilation, and supportive care. Pigs were positioned in dorsal recumbency. A median saphenous artery was catheterized for direct arterial pressure management. Each tibia was surgically scrubbed and a NIRS sensor (Nonin, Plymouth, MN) placed over the craniolateral muscle compartment. On the test leg of all pigs, 2 18-gauge needles were centered on each side of the sensor, angled 20° toward the center. Proximal and distal needles were used for 5% albumin infusion to manually elevate tibial intra-compartmental pressures (TICP). Cranial and caudal needles were used for direct pressure transducer measurement of TICP by averaging the values. An 18 gauge needle on the lateral aspect of the control leg sensor measured TICP via direct pressure transducer. Continual time synchronized measures of systolic (SAP), diastolic, and mean pressures (MAP), pulse rate, respiratory rate, systemic pulse oximetry, body temperature, TICP, and NIRS from each leg were collected. For the control group, transducers were zeroed and TIPP of the test leg was incrementally increased by albumin infusion. Measurements were taken at baseline for 10 min, TIPP=40, 30, 20, and 10 mmHg for 5 min each, TIPP=0 mmHg for 10 min, TIPP equal to MAP for 10 min, SAP for 10 min and SAP+10 mmHg for 10 min. Fasciotomies were then performed and measurements taken for 10 additional min. All pigs were euthanized at the end of the experiment. For the acute trauma group, instrumentation was marked and removed from the test leg after the 10 min baseline period. The limb was stabilized and trauma induced by dropping a 2kg weight 30 times down a 100 cm high cylindrical tube on the craniolateral compartment. Instrumentation was replaced and a 45 minute equilibration period observed before the infusion protocol was performed as described above. The contralateral (non-traumatized) leg was used as an internal control. For each group, a repeated measures ANOVA model, including factors for group, time, and group by time interaction, tested for differences in TICP, TIPP and NIRS values. All tests were 2-sided with $\alpha<0.05$ considered significant. Pearson's correlations were calculated between TICP and NIRS, and TIPP and NIRS. **Results:** Both models created consistent, reproducible increases in TICP and decreases in TIPP. Significant increases in TICP between test and control limbs were found at all time points except TIPP=40mmHg and 5 and 10 min following fasciotomies. NIRS was able to detect significant changes in tissue oxygenation at all the same time points. All TICP of the test leg increased significantly from baseline except for 10 min following fasciotomy. Once TIPP reached 20mmHg, NIRS decreased significantly from baseline and did not return to baseline levels until 5 and 10 min after fasciotomies. NIRS was able to detect decreased oxygenation at every TIPP decrease and subsequent increase following fasciotomies. TIPP was significantly different than baseline at all time points until 5 min after fasciotomies. Similar TIPP and TICP were observed among non-traumatized and traumatized test limbs, with the exception that traumatized test limb NIRS were significantly lower immediately after the trauma event. Significant negative correlations of TICP and NIRS (trauma: $r=.70$, $p<.0001$; controls: $r=-.79$, $p<.0001$) and positive correlations of TIPP and NIRS (trauma: $r=.70$, $p<.0001$; controls: $r=.80$, $p<.0001$) were observed. **DISCUSSION:** NIRS provided a reliable, sensitive measure correlating to both an increase and decrease in TICP and TIPP, respectively, in this model. The addition of acute trauma to the model did not alter the correlations of NIRS values with TICP and TIPP. Despite 70 min of TIPP that were significantly below baseline, oxygenation returned to normal after fasciotomy, suggesting no permanent muscle damage. Further research is needed to determine at what NIRS reading a fasciotomy may be indicated to prevent permanent tissue damage.

NIRS vs Direct Pressure Monitoring of Acute Compartmental Syndrome in a Porcine Model

Curtis Cathcart, Michael Shuler, Brett Freedman, Lisa Reynolds, Ashley Cole, Thomas Whitesides, Emily Smith, Steven Budsberg

Purpose: Acute compartment syndrome (ACS) can have devastating sequelae if missed or if treatment is delayed. Near infrared spectroscopy (NIRS) has been proposed for continual, non-invasive monitoring of traumatized extremities. This study sought to correlate NIRS and the tibial intra-compartmental perfusion pressure (TIPP) in a porcine model of ACS. **Methods:** The study consisted of Landrace swine divided into two groups: control (N=16) and acute trauma (N=15). All pigs were maintained on isoflurane with positive pressure ventilation, and supportive care. Pigs were positioned in dorsal recumbency. A median saphenous artery was catheterized for direct arterial pressure management. Each tibia was surgically scrubbed and a NIRS sensor (Nonin, Plymouth, MN) placed over the craniolateral muscle compartment. On the test leg of all pigs, 2 18-gauge needles were centered on each side of the sensor, angled 20° toward the center. Proximal and distal needles were used for 5% albumin infusion to manually elevate tibial intra-compartmental pressures (TICP). Cranial and caudal needles were used for direct pressure transducer measurement of TICP by averaging the values. An 18 gauge needle on the lateral aspect of the control leg sensor measured TICP via direct pressure transducer. Continual time synchronized measures of systolic (SAP), diastolic, and mean pressures (MAP), pulse rate, respiratory rate, systemic pulse oximetry, body temperature, TICP, and NIRS from each leg were collected. For the control group, transducers were zeroed and TIPP of the test leg was incrementally increased by albumin infusion. Measurements were taken at baseline for 10 min, TIPP=40, 30, 20, and 10 mmHg for 5 min each, TIPP=0 mmHg for 10 min, TIPP equal to MAP for 10 min, SAP for 10 min and SAP+10 mmHg for 10 min. Fasciotomies were then performed and measurements taken for 10 additional min. All pigs were euthanized at the end of the experiment. For the acute trauma group, instrumentation was marked and removed from the test leg after the 10 min baseline period. The limb was stabilized and trauma induced by dropping a 2kg weight 30 times down a 100 cm high cylindrical tube on the craniolateral compartment. Instrumentation was replaced and a 45 minute equilibration period observed before the infusion protocol was performed as described above. The contralateral (non-traumatized) leg was used as an internal control. For each group, a repeated measures ANOVA model, including factors for group, time, and group by time interaction, tested for differences in TICP, TIPP and NIRS values. All tests were 2-sided with $\alpha<0.05$ considered significant. Pearson's correlations were calculated between TICP and NIRS, and TIPP and NIRS. **Results:** Both models created consistent, reproducible increases in TICP and decreases in TIPP. Significant increases in TICP between test and control limbs were found at all time points except TIPP=40mmHg and 5 and 10 min following fasciotomies. NIRS was able to detect significant changes in tissue oxygenation at all the same time points. All TICP of the test leg increased significantly from baseline except for 10 min following fasciotomy. Once TIPP reached 20mmHg, NIRS decreased significantly from baseline and did not return to baseline levels until 5 and 10 min after fasciotomies. NIRS was able to detect decreased oxygenation at every TIPP decrease and subsequent increase following fasciotomies. TIPP was significantly different than baseline at all time points until 5 min after fasciotomies. Similar TIPP and TICP were observed among non-traumatized and traumatized test limbs, with the exception that traumatized test limb NIRS were significantly lower immediately after the trauma event. Significant negative correlations of TICP and NIRS (trauma: $r=.70$, $p<.0001$; controls: $r=-.79$, $p<.0001$) and positive correlations of TIPP and NIRS (trauma: $r=.70$, $p<.0001$; controls: $r=.80$, $p<.0001$) were observed. **DISCUSSION:** NIRS provided a reliable, sensitive measure correlating to both an increase and decrease in TICP and TIPP, respectively, in this model. The addition of acute trauma to the model did not alter the correlations of NIRS values with TICP and TIPP. Despite 70 min of TIPP that were significantly below baseline, oxygenation returned to normal after fasciotomy, suggesting no permanent muscle damage. Further research is needed to determine at what NIRS reading a fasciotomy may be indicated to prevent permanent tissue damage.

SCIENTIFIC ARTICLE

Ability of Near Infrared Spectroscopy to Measure Oxygenation in Isolated Upper Extremity Muscle Compartments

Ashley L. Cole, MPH, Richard A. Herman Jr, BS, Jonathan B. Heimlich, BS, Sahir Ahsan, BS, Brett A. Freedman, MD, Michael S. Shuler, MD

Purpose Near infrared spectroscopy (NIRS), a noninvasive means for monitoring muscle oxygenation, may be useful in the diagnosis of acute compartment syndrome, a condition characterized by poor tissue perfusion. This study used the decrease in muscle oxygenation caused by exercise to investigate the ability of anatomic placement of NIRS sensor pads over compartments of the forearm to isolate perfusion values of a specific compartment.

Methods We recruited 63 uninjured volunteers from a private clinic-based setting and placed NIRS sensor pads over the dorsal, volar, and mobile wad compartments of 1 forearm. A total of 49 participants also had the contralateral forearm monitored, which served as an internal control. Participants performed a series of 3 exercises designed to sequentially activate the muscles of each compartment. A washout period separated each exercise to allow perfusion to return to baseline. We compared NIRS values of each compartment recorded during muscle contraction with baseline values.

Results Mean NIRS values decreased significantly from baseline during muscle contraction for all compartments, whereas mean NIRS values of muscle compartments that remained at rest showed little or no change. We observed no changes in NIRS values of the contralateral arm, which remained at rest during the entire data collection period.

Conclusions Although lack of an existing method for quantifying muscle perfusion precludes validation of this technique against a reference standard, this study suggests that NIRS can provide oxygenation values that are both sensitive and specific to muscle compartments of the forearm. Future studies should investigate NIRS among patients with upper extremity injuries. *(J Hand Surg 2012;37A:297–302. Copyright © 2012 by the American Society for Surgery of the Hand. All rights reserved.)*

Type of study/level of evidence Diagnostic III.

Key words Acute compartment syndrome, compartment syndrome, muscle perfusion, near infrared spectroscopy.

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Somanetics Corporation supplied INVOS devices used in this study. M.S.S. has pending intellectual property rights and a license agreement with the manufacturer.

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Acute compartment syndrome (ACS), a condition that results from inadequate perfusion in an injured extremity, causes devastating sequelae if not promptly diagnosed and treated. To date, the only objective diagnostic technique available to clinicians is intramuscular pressure measurement. However, these measurements are invasive and painful, and if performed incorrectly may yield unreliable results.[1–3]

Near infrared spectroscopy (NIRS)–based tissue monitors use differential light absorption characteristics to provide a noninvasive, continuous means to quantify the proportion of hemoglobin saturated with oxygen in tissue 2 to 3 cm beneath the skin.[4–7] The US Food and Drug Administration has validated and approved NIRS to monitor perfusion of cerebral and somatic tissue below the sensors. Near infrared spectroscopy is capable of passing through skin, soft tissue, and bone. The depth of penetration is directly proportional to the distance or separation between the light source and light receptor.[6,7] With the sensor used in this study, complete absorption of light by large vessels and hematomas means that the light collected by NIRS sensors is light that is capable of passing through the microcirculation.[4] Because they allow for measurement of perfusion, the critical factor in compartment syndrome, devices using NIRS technology may be useful for detecting ACS.

Near infrared spectroscopy–based tissue perfusion monitors use noninvasive sensor pads that emit 1 to 4 beams of red light, which are used to measure muscle oxygenation. It is necessary to monitor each muscle compartment because a compartment syndrome can develop in one compartment and not another. Because these sensor pads are placed on the surface of the skin, proper placement is essential to obtain an accurate reading.

Previous studies[4,8–10] have validated the responsiveness of NIRS to changes in muscle oxygenation of the forearm. However, for NIRS to be validated for clinical practice, it must also be demonstrated that pad placement produces the oxygenation values of the intended compartment without any cross-contamination or interference from neighboring compartments. To this end, we designed a study that sought to investigate the ability of NIRS to determine whether measurements of muscle oxygenation in a single compartment can be determined independently of other compartments. We did this by measuring the decrease in tissue oxygenation caused by muscle contraction, 1 compartment at a time, while measuring the response in all compartments. We hypothesized that NIRS values of the activated compartment would decrease significantly from baseline, whereas the values of the compartments at rest would remain largely unaffected.

MATERIALS AND METHODS

The study population consisted of 63 uninjured volunteers between 18 and 75 years of age, who provided written informed consent in accordance with institutional review board approval. We recruited study participants using a mass e-mail that solicited volunteers from a pool of employees and members of the local community. Exclusion criteria included subjects with a diagnosis of peripheral vascular disease or pulmonary disease, or prior surgery of the forearm other than wrist surgeries such as carpal tunnel or first dorsal compartment release.

Once we enrolled subjects, we recorded their age, gender, race, and body mass index (BMI). We obtained NIRS values using an INVOS Cerebral Oximeter (Model 5100; Somonetics, Troy, MI). Values are displayed as the percentage of hemoglobin saturated with oxygen (rSO_2). Consequently, a higher reading indicates a higher tissue oxygenation level. The device was calibrated during manufacturing and did not need recalibration before use.

All patients lay in a supine position, and we placed NIRS sensors over the volar, dorsal, and mobile wad muscle compartments at the junction of the proximal third and middle third of each forearm, 7 to 10 cm from the elbow. We measured the volar compartment by placing a pad over the superficial flexor muscles. We accessed the dorsal compartment by palpating the ulna. Then, we placed a pad 1 to 2 cm dorsally, over the extensor carpi ulnaris muscle. To locate the mobile wad, we asked participants to flex the elbow while receiving resistance at the wrist to reveal the brachioradialis muscle. We placed a pad directly over the brachioradialis muscle. We obtained baseline rSO_2 values after participants had been at rest for 60 seconds to allow readings to stabilize. We did not specifically examine the pronator quadratus and deep flexor compartments in this study.

To sequentially isolate each of these 3 compartments, the participant was asked to perform exercises designed to activate the desired muscle group, resulting in a predictable decrease in muscle oxygenation. We tailored each exercise specifically to activate muscles of a specific compartment while muscles of other compartments remained at rest. All exercises were performed with the elbow resting on the examination table at a right angle and the shoulder at rest. The participant performed each exercise for 30 to 60 seconds, followed

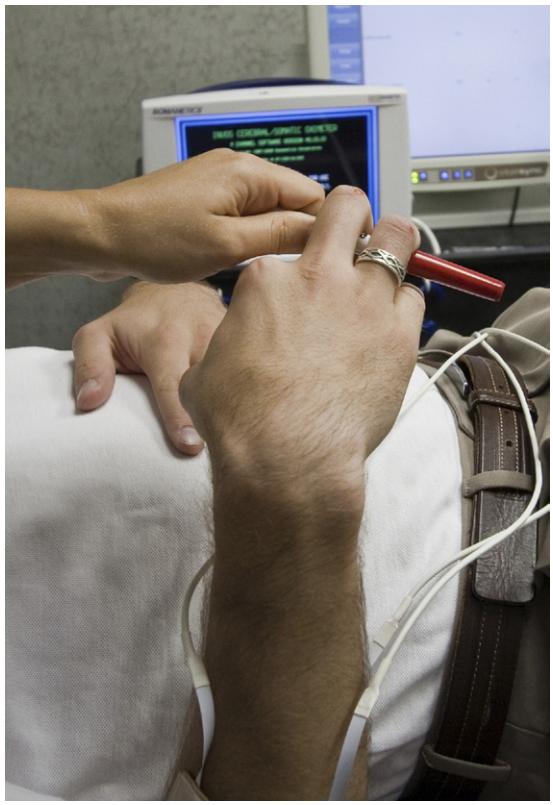

FIGURE 1: To isolate the flexor digitorum superficialis in the volar compartment, subjects flexed the middle and ring fingers around a writing pen against resistance offered by the researcher while relaxing the rest of the hand.

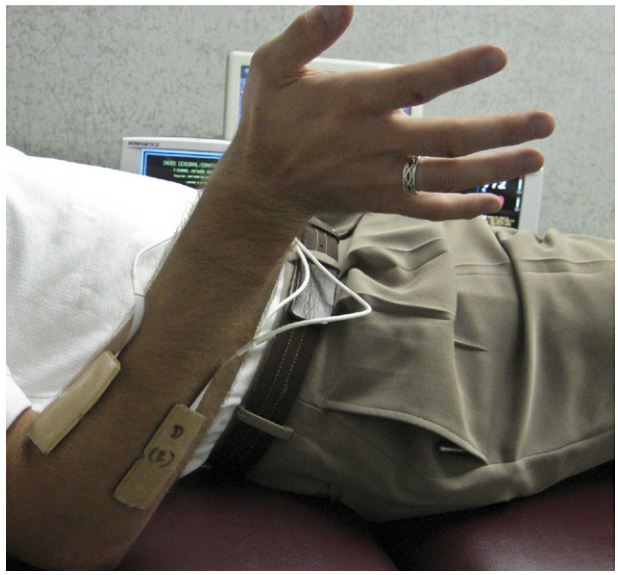

FIGURE 2: To activate the extensor carpi ulnaris in the dorsal compartment, subjects extended the wrist and fingers with the palm facing the ceiling.

by a washout period of 60 seconds, to allow the subject's rSO_2 values to return to baseline.

To activate the volar compartment, we instructed subjects to flex the middle and ring fingers around a writing pen against resistance offered by a member of the research team, while relaxing the rest of the hand. The goal was to isolate and test the flexor digitorum superficialis (Fig. 1). To activate the dorsal compartment, participants extended the wrist and fingers with the elbow bent at 90°, the palm faced toward the ceiling, and the fingers extended. This movement activated the extensor carpi ulnaris (Fig. 2). To activate the mobile wad (brachioradialis), with the wrist facing medially, the participant flexed at the elbow against resistance supplied by an investigator, while keeping the hand and wrist relaxed (Fig. 3). We instructed participants to give 75% effort during constant contraction for roughly 30 seconds.

Among a subset of patients, we monitored the contralateral upper extremity as well. The contralateral arm remained at rest during all muscle activation of the test arm. The contralateral side was validated previously as

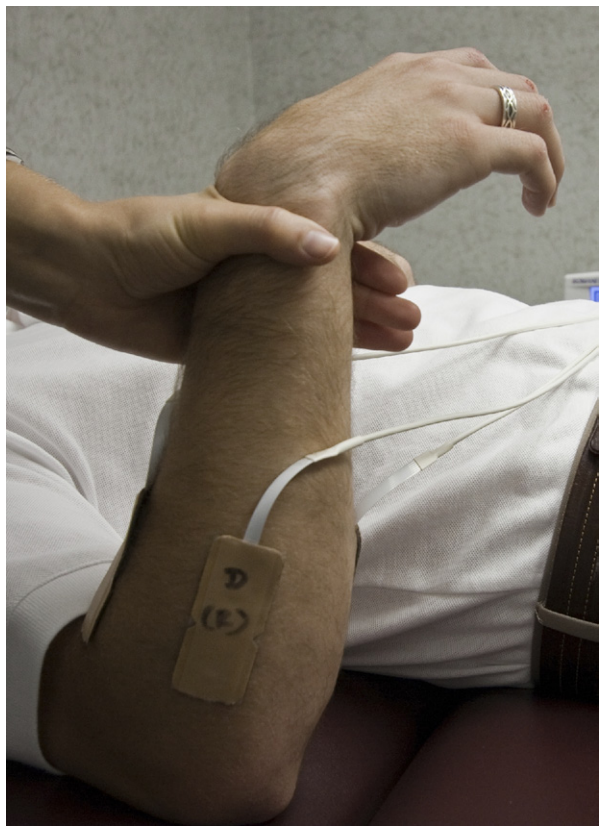

FIGURE 3: To activate the brachioradialis of the mobile wad compartment, subjects flexed the elbow against resistance offered by the researcher while keeping the hand and wrist relaxed.

TABLE 1. Mean and Interquartile Range for NIRS (rSO_2) Values From Each Muscle Compartment of the Forearm Among 63 Volunteers, Before and After Muscle Contraction

	Volar	Dorsal	Mobile Wad
Baseline	**79.5 (73, 86)**	69.4 (64, 75)	73.9 (69, 75)
Fatigue	**53.4 (42, 69)**	66.0 (62, 72)	72.5 (68, 78)
Change	**−26.1 (−37, −13)**	−3.4 (−8, 1)	−1.3 (−5, 3)
P value	**<.0001**		
Baseline	80.3 (76, 86)	**69.4 (65, 74)**	74.5 (72, 80)
Fatigue	81.4 (79, 88)	**35.0 (18, 48)**	74.9 (71, 80)
Change	1.1 (−1, 3)	**−34.4 (−46, −24)**	0.3 (−2, 4)
P value		**<.0001**	
Baseline	83.6 (80, 91)	72.5 (67, 79)	**75.2 (71, 80)**
Fatigue	81.6 (77, 87)	67.4 (64, 74)	**48.3 (41, 60)**
Change	−2.1 (−4, 1)	−5.1 (−8, 1)	**−26.8 (−36, −14)**
P value			**<.0001**

Values are presented as percent oxygenation; values from stimulated compartments are shown in bold. *P* values are for signed rank test.

an internal control for NIRS monitoring in the lower extremity.[5]

We calculated the response to muscle contraction for each compartment of the forearm as the change in rSO_2 values from baseline (rSO_2 value during muscle contraction minus rSO_2 value at rest). We tested mean differences between rSO_2 values at baseline and during muscle contraction for significance using the signed rank test and considered results to be statistically significant at $P \leq .05$. We assessed normality using the Anderson-Darling test.

RESULTS

Of 63 uninjured study participants, 52 were female. Most participants were nonsmokers (58 participants) and nondiabetic (61 participants). A total of 28 participants were of normal weight (BMI $<$ 25), 15 were overweight (BMI between 25 and 29), and 19 were obese (BMI $\geq$ 30).

Table 1 presents the rSO_2 values for each compartment. All rSO_2 values of activated compartments decreased significantly from baseline during muscle contraction ($P<.0001$ for all compartments), whereas compartments at rest remained largely unchanged.

Figure 4 shows perfusion data from each muscle compartment of a sample study participant throughout sequential muscle contraction and washout periods. Activation of each compartment is labeled with an arrow.

For 49 study participants, rSO_2 values were available for the contralateral forearm. Table 2 presents a comparison of rSO_2 values from each arm at baseline and after muscle activation of a given compartment. In the activated arm, rSO_2 values decreased by an average of approximately 25 percentage points during muscle contraction, whereas the average change in values from the contralateral arm was approximately 0.

We observed no differences in rSO_2 values by gender or BMI. The current study sample precluded stratification by diabetes or smoking status.

DISCUSSION

Near infrared spectroscopy provides the potential for noninvasive, continuous monitoring of tissue perfusion, which could provide a useful objective means of diagnosis of ACS. However, for this technology to be validated, one must be confident that anatomic placement of NIRS sensor pads on the surface of the skin produces values of the intended muscle compartment.

This study measured rSO_2 values during sequential contraction of muscles in each of the 3 traditionally recognized compartments of the forearm among 63 uninjured volunteers. The results suggest that the pad placement described here produces rSO_2 values that are both sensitive and specific to the intended compartment. During muscle contraction of each compartment, mean rSO_2 values decreased significantly from values taken while the participant was at rest, reflecting the decrease in tissue oxygenation induced by exercise. Moreover, mean rSO_2 values of surrounding (unstimulated) muscle compartments reflected little or no change, suggesting the ability of NIRS to produce measurements specific to the intended compartment.

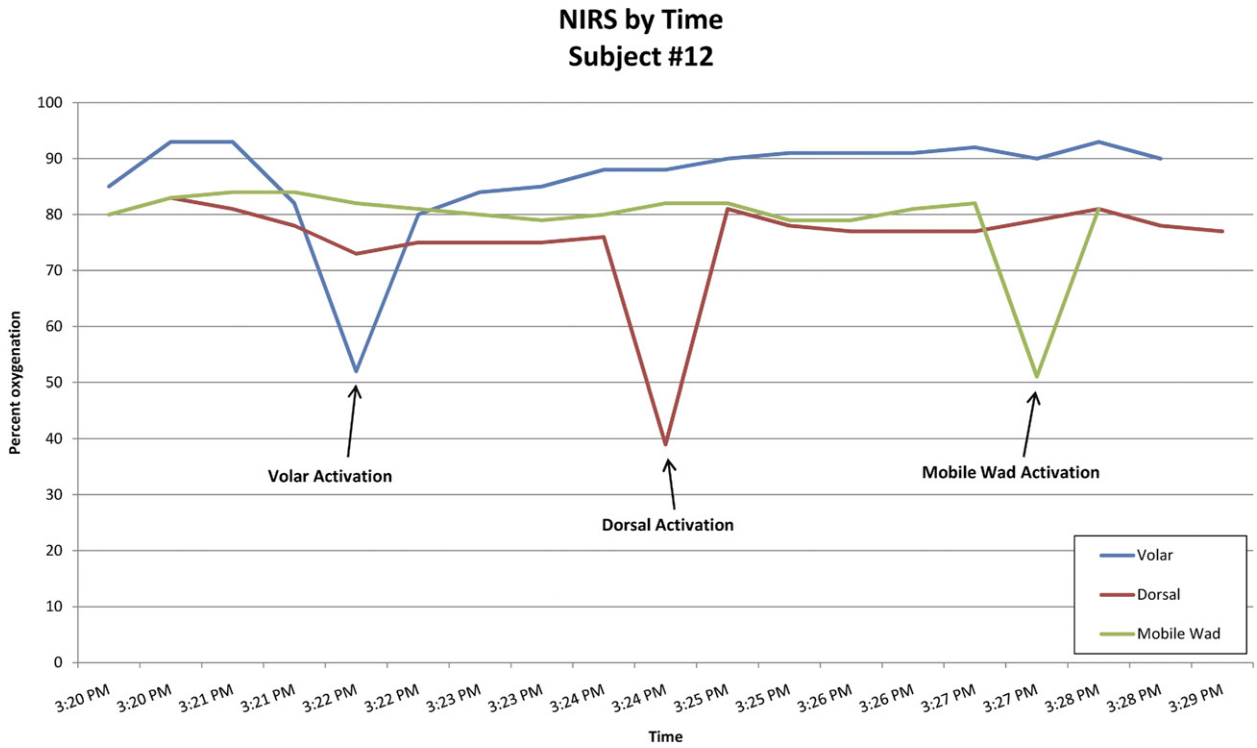

FIGURE 4: An example of the response to muscle oxygenation measured by NIRS for a sample participant. Arrows show sequential activation of each compartment.

A subset of participants had both the activated and contralateral arms monitored. Whereas values of the test arm substantially decreased as a result of muscle contraction, mean values collected simultaneously from the control arm showed no clinically meaningful change. These results suggest that decreases observed during muscle contraction were not spontaneous, because we did not observe similar changes in the contralateral arm.

Owing to an amendment to data collection procedures, only 49 of the 63 subjects provided NIRS values from the contralateral arm; however, results from this subsample support the hypothesis that values of compartments of a forearm at rest remain stable.

One major obstacle in the validation of NIRS is the lack of another noninvasive method of measuring muscle perfusion. This precludes traditional validation of this technique against a reference standard or true value. Without such a true value, manipulation of muscle oxygenation of an isolated compartment is the only way to confirm that rSO_2 values produced belong to the intended compartment and not its neighbor. Nevertheless, there may have been some unintended activation of surrounding muscle groups, because it can be difficult for a participant to isolate a particular muscle. Furthermore, lack of a standard prevents traditional calculations of sensitivity and specificity rates; never-

TABLE 2. Mean and IQR of NIRS (rSO_2) Values From Test and Contralateral (Control) Compartments of the Upper Extremity Among 49 Volunteers, at Baseline and in Response to Muscle Contraction

	Test Arm		Control Arm	
	Pre	Post	Pre	Post
Volar				
Mean	78.8	56.6	76.8	78.3
IQR	72, 86	44, 69	72, 82	72, 84
Difference	−21.7 (−32, −12)		1.5 (0, 3)	
Dorsal				
Mean	68.2	37.0	70.4	71.8
IQR	65, 72	19, 48	66, 77	67, 78
Difference	−34.8 (−49, −24)		1.4 (0, 2)	
Mobile wad				
Mean	73.9	50.4	74.2	75.0
IQR	70, 79	43, 59	72, 78	72, 80
Difference	−24.6 (−34, −14)		0.8 (0, 1)	

IQR, interquartile range.
"Pre" and "Post" refer to rSO_2 values taken at baseline and after muscle contraction, respectively. Values are presented as percent oxygenation.

theless, the results of this study demonstrate the concepts of sensitivity and specificity through the observed responses to exercise on activated and nonactivated muscle compartments, respectively.

This study provides evidence supporting further investigation of the use of NIRS as a noninvasive, continual monitoring tool for ACS of the forearm, but there are some inherent limitations to this application. There are reports of elevation of tissue pressures within subcompartments, the perfusion of which NIRS may not be capable of reading. In addition, the NIRS device used in this study measures oxygenation in the microcirculation 2 to 3 cm beneath the skin. Thus, it is plausible that subcutaneous fat exceeding 2 to 3 cm at the sensor site may impede the device's ability to obtain a reading. Although we encountered no such difficulties in this study, this concern warrants investigation in a future study. Moreover, because of complete light absorption in this particular device, NIRS is not currently capable of obtaining perfusion values in the presence of a hematoma; nevertheless, NIRS light is able to penetrate skin, soft tissue, and bone. Future studies should focus on the use of NIRS in a clinical setting to investigate and address these and other limitations.

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Correlation of near infrared spectroscopy (NIRS) and direct pressure monitoring in an acute porcine compartmental syndrome model

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Objective: To correlate near infrared spectroscopy (NIRS) and the tibial intra-compartmental perfusion pressure (TIPP) in an acute limb compartmental syndrome (ALCS).

Methods: Landrace swine subdivided into 2 groups, control (N=16) and acute trauma (N=15). NIRS sensors were placed over the craniolateral muscle compartment of proximal both tibiae. Albumin infusion elevated tibial intra-compartmental pressures (TICP). Time synchronized measures of systolic (SAP), diastolic (DAP) and mean pressures (MAP), TICP, and NIRS from each leg were collected. For the acute trauma group, trauma was induced by dropping a 2kg weight 30 times from100 cms directly on the muscle compartment. For each group, a repeated measures ANOVA model was used to test differences in TICP, TIPP and NIRS values. Pearson's correlations were calculated between TICP and NIRS, and TIPP and NIRS.

Results: Both models created reproducible increases in TICP and decreases in TIPP. Trauma did not alter TICP, TIPP or NIRS measurements in the model. NIRS was able to detect significant changes in tissue oxygenation at all the same time points. NIRS was able to detect decreased oxygenation at every TIPP decrease and subsequent increase following fasciotomies. An increase in NIRS was seen in all cases once fasciotomy was performed and TICP was reduced.

Conclusions: NIRS provided a sensitive measure correlating to both an increase and decrease in TICP and TIPP, respectively, in this infusion model. The addition of acute trauma to the model did not alter the correlations of NIRS values with TICP and TIPP. Fasciotomy produced a rebound in NIRS values.

Introduction

Over the last two decades, tissue oxygenation saturation (StO_2) measured by near infrared spectroscopy (NIRS) has been extensively evaluated for use in determining systemic and regional tissue perfusion (1-4). It is widely used, and validated for monitoring cerebral oxygenation during anesthesia (5-7). Recent efforts have focused on this use of NIRS in assessing regional perfusion and more specifically regional perfusion in the setting of acute limb compartmental syndrome [ALCS] (8-11). Current objective measures of compartment health in ALCS focus on intra-compartmental pressure, as a proxy for perfusion of the tissue. The invasive measurement of pressure within the limb compartment in question provides indirect data on the physiological state of the limb compartment. This technique has been used for decades and recommendations for fasciotomy (the universally accepted treatment for ALCS) exist that are based upon both absolute intra-compartmental pressure (ICP) and differential pressure (perfusion pressure or PP) [diastolic arterial pressure – ICP] (12-15). Animal and human studies have explored different aspects of ACLS as well as a variety of NIRS setting for potential use in ALCS (13,16-24). Studies have suggested when PP drops below 20 to 10 mmHg tissue ischemia occurs and justifies fasciotomy (18, 25, 26) Correlating continuous NIRS monitoring of the compartment with PP may help guide clinicians with treatment decisions as well as creating prognostic data via StO_2 measurements. Two studies in a porcine model of ALCS in the proximal craniolateral tibial compartment showed correlations of ICP with NIRS, and documentation of significantly different levels of StO_2 measured by NIRS in hypotension, hypotension and hypoxeia (with and without increased ICP) respectively(16,17). In each study ALCS was defined as a loss of muscle twitch during peroneal nerve stimulation but interestingly mean ICP varied greatly. Neither study found an ICP predictive of muscle twitch cessation and

furthermore there is no data suggesting that either ICP or PP values indicated reversible or irreversible tissue injury in the limb compartment. Additionally, none of the research or clinical models to date have addressed the potential concerns of NIRS measurement variability in the presence of trauma induced tissue edema or hemorrhage.

The goal of this study was to correlate ICP and PP with NIRS through a wide range of ICP and PP values in an acute porcine model and to determine if blunt force trauma to the limb would alter these correlations using a commercially available NIRS device. The hypotheses tested were that ICP and PP would have correlations with NIRS throughout a wide range of pressures and that acute blunt force trauma would not alter NIRS values or the associated correlations with compartment pressures.

Materials and Methods

Animals – Thirty one landrace swine (48-68 kg) were used in the study (IACUC # A2010 1-012).

Study Design – Pigs were divided into a control group of 16, and an acute trauma group of 15 animals. All pigs underwent the same experimental procedures and monitoring setup as described herein. Pigs were maintained on isoflurane (IsoFlo®, Abbott Laboratories, North Chicago, IL 60064 USA) with mechanical positive pressure ventilation. A circulating warm water pad maintained rectal body temperatures between 98 and 101 degrees Fahrenheit. A 20 gauge intravenous catheter was placed in an auricular vein for constant infusion of lactated ringer's solution (Veterinary Lactated Ringer's Injection USP, Abbott Laboratories, North Chicago, IL 60064) at 5 ml/kg/hr. Pigs were positioned in dorsal (supine) recumbency. Surgical cut downs exposed a median femoral artery for direct arterial pressure measurement, and the

right jugular and femoral vein for blood sampling of the test leg via 18 gauge catheters. Both hind limbs (from stifle to tarsus) were clipped of hair, cleaned with 4% chlorhexidine scrub (2% Chlorhexidine Gluconate, First Priority Inc., Eglin, IL 60123-1146) and alcohol (70%). NIRS self adhesive sensors (EQUANOX^{TM} Sensor, Model 8003CA, Nonin Medical, Inc., Plymouth, MN) were placed on the skin overlying the muscles of the craniolateral compartment of each leg (i.e. test and control legs of both the control and trauma groups), such that at least 1 cm of craniolateral compartment musculature extended proximal, cranial and caudal to the sensor. On the test leg, four 18 gauge needles were placed at the periphery, centered on each side of the sensor and angled 20 degrees toward the center of their tips were in the field monitored by the NIRS sensor (Figure 1). The proximal and distal needles were attached via a T-connection for infusion of 5% human albumin (AlbuRx^{TM} 5, CSL Behring AG, Bern, Switzerland) to manually elevate the compartmental pressure at predetermined intervals in the test legs. The cranial and caudal needles were used for direct pressure transducer measurement of compartmental pressure by averaging the values. On the control legs, a single 18 gauge needle was placed on the lateral aspect of the NIRS sensor for direct pressure transducer measurement of compartmental pressure. Continual time synchronized measurements of systemic blood pressure – systolic (SAP), diastolic (DAP), and mean pressures (MAP), pulse rate, respiratory rate, systemic pulse oximetry, body temperature, compartmental pressures (2 transducers on test leg (averaged) and one on control leg), and regional oximetry (NONIN EQUANOX^{TM} 7600 Oximeter, Nonin Medical, Inc., Plymouth, MN) from the NIRS sensors from each leg were collected. Once compartmental transducers were zeroed, tibial intra-compartmental perfusion pressure (TIPP) of the test leg was increased in increments by albumin infusion. Measurements were taken at baseline (0 mm Hg) for 10 minutes, TIPP of 40 mm Hg for 5 minutes, TIPP of 30 mm Hg for 5

minutes, TIPP of 20 mm Hg for 5 minutes, TIPP of 10 mm Hg for 5 minutes, TIPP of 0 mm Hg for 10 minutes, TIPP equal to MAP for 10 minutes, TIPP equal to SAP for 10 minutes and TIPP equal to SAP + 10 mm Hg for ten minutes. At this time fasciotomies were performed and measurements taken for an additional 10 minutes. The first fasciotomy was performed by sharp incision caudolateral of the NIRS sensor from stifle to hock to a depth through fascial layers of the muscular compartment. If there was not an immediate (within 60 seconds) increase in NIRS, a second fasciotomy was performed in a similar manner along the craniolateral aspect of the tibia.

The acute trauma group of 15 pigs were maintained on isoflurane with mechanical positive pressure ventilation using an identical protocol as the control group. NIRS sensors were placed over the craniolateral compartment of each hindlimb in all animals as described above.. The continuous time-synchronized measures, as in the control group, were recorded for both legs for 10 minutes to establish baseline. After equilibration, the location of the 18 gauge needles and NIRS sensor on the leg was marked and the instrumentation removed. The craniolateral musculature on the test leg was then traumatized in the following manner: the craniolateral compartment was positioned by slightly internally rotating the test hind limb which was held in place using an Olympic Vac-Pac® patient positioning system. Once placed around the leg, this system became rigid when vacuum was applied, effectively holding the leg in a stable position until trauma induction was complete. Next a 2 kg weight was dropped down a vertically orientated cylindrical tube 30 times from a 100 cm height. A plumb bob attached to the outside ensured the apparatus was vertical for each drop. The measurement instrumentation was replaced on the test leg immediately after trauma induction and a 45 minute equilibration period was recorded before start of colloid infusion (5% human albumin). The contralateral leg was used as

an internal control and was not traumatized. An identical testing protocol including increasing intra-compartmental pressure and monitoring was performed. All pigs were euthanized at the end of the experiment with an intravenous injection of pentobarbital sodium (Beuthanasia® –D Special, Schering-Plough Animal Health Corp., Union, New Jersey 07083). Total time of altered TIPP was 70 minutes.

Statistical Analysis - A repeated measures model that recognized multiple observations was used to test for differences in tibial intra-compartmental pressure (TICP), TIPP and NIRS values between test and control limbs and time points in both groups. The full model included factors for group, time point and a group by time point interaction. Multiple comparisons were adjusted for using Tukey's test. All hypothesis tests were 2-sided and the significance level was $\alpha = 0.05$. Pearson's correlations were calculated between TICP and NIRS measurements and between TIPP and NIRS.

Results

In both groups (control and acute trauma), the model created consistent, reproducible increases in TICP and decreases in TIPP (Figures 2-5). No significant differences in TICP, TIPP or NIRS were seen between control and acute trauma groups at all time periods during the experiment. Significant increases in TICP between test and control limbs were found at all time points except TIPP=40mmHg and 5 and 10 minutes following fasciotomies. NIRS was able to detect significant changes in tissue oxygenation at all the same time points. All TICP of the test leg increased significantly from baseline except for 10 minutes following fasciotomy. Once TIPP reached 20mmHg, NIRS decreased significantly from baseline and did not return to baseline

levels until 5 to 10 minutes after fasciotomies (Figures 3&5). NIRS was able to detect decreased oxygenation at every TIPP decrease and subsequent increase following fasciotomies. TIPP was significantly different than baseline at all time points until 5 minutes after fasciotomies. Similar TIPP and TICP were observed among control and acute trauma test limbs, with the exception that acute trauma test limb NIRS values were significantly lower immediately after the trauma event. Significant negative correlations of TICP and NIRS (trauma: $r= -0.74$, $p<0.0001$; controls: $r=-0.79$, $p<0.0001$) and positive correlations of TIPP and NIRS (trauma: $r=0.76$, $p<.0001$; controls: $r=0.80$, $p<0.0001$) were observed.

In both groups, the initial caudolateral fasciotomy was performed by sharp incision caudolateral to the NIRS sensor from stifle to hock to a depth through all fascial layers of the muscular compartment. In the control group, seven pigs did not have an immediate increase in NIRS and a second fasciotomy was performed (Table 1). Similarly, in the acute trauma group eleven pigs received a second fasciotomy. Thus NIRS was able to detect decreased tissue oxygenation at every perfusion pressure decrease and subsequent increase following pressure relieving fasciotomies. TIPP pressures were significantly different than baseline at all time points until 5 minutes after fasciotomies. Despite 70 minutes where perfusion pressures were significantly below baseline, tissue oxygenation returned to normal values after compartmental pressure release (Figure 5).

Discussion

The current data supported the hypotheses tested in the study. NIRS had significant correlations to both ICP and PP throughout a wide range of pressures in the tibial muscle

compartment. Additionally NIRS was not altered by the addition of acute blunt force trauma to the model or the associated correlations with compartment pressures. These results confirm that NIRS can provide a viable real time method of longitudinal sampling of assessing regional perfusion and more specifically regional perfusion in the setting of acute limb compartmental syndrome. These data provide new insight into this relationship as previous articles had no correlation to PP since synchronized measurements with systemic blood pressure were absent and PP could not be calculated (16,17). The lack of change in NIRS values for the trauma group contrasts a finding of Shuler et al (20) in which in a series of tibial fracture cases showed increased NIRS values peripheral to the fracture site. The difference between these results may be due to the mode and severity of limb trauma and exact sites measured. In this model, NIRS values were measured only directly over the traumatized tissue and not peripherally as was done previously.

Data from this study suggests that NIRS may have a role in determining a threshold level of a specific outcome measure that can assist the clinician's decision whether or not to perform a fasciotomy. It was noted that NIRS values dropped significantly from baseline at a TIPP of 20 mm Hg or less in both the control and acute trauma test limbs. Thus, NIRS is able to detect differences in oxygenation at TIPP considered to be diagnostic for ALCS and a threshold for fasciotomy (16, 17) . While these data do not suggest nor document any effect on the muscle tissue, they do provide evidence for a future avenue of work.

The data involving the fasciotomies also provided some interesting results. While there is no way to know if the limbs that did receive a second fasciotomy would have had improved PP and higher NIRS values over time without the second fasciotomy, the NIRS provided real time data that could be used to assess if the initial fasciotomy was successful in releasing intra-

compartmental pressure and restoring muscle perfusion. This finding has implications as a potential use of NIRS intra-operatively as a quality control device to insure adequate release of the compartments to prevent insufficient releases (15).

A second finding was that in limbs of both pigs groups where a second fasciotomy was performed, TIPP could improve toward baseline initially without a NRIS change up to a certain point. As shown in the results during this time, the NIRS was not changing and thus the decision to perform the second fasciotomy was made. While current data documents there is a direct relationship of TIPP to NIRS, the NIRS values may be more sensitive in the initial attempts at compartmental decompression as it assesses the tissue oxygenation and not merely an arbitrary change in pressure.

A second point of potential difference between current data and previous studies using this model exists (16, 17). Landrace pigs used in the current study were larger (40 to 45 kgs) and allowed for measurement of a tibial compartment with depths to 25 millimeters. Previous studies (16, 17) used smaller Landrace pigs (13 to 18kgs); pigs of similar size had measured tibial compartments size with depths of 8-12 mm. Given the fact that the sensor is calibrated over a 25 millimeters depth, it is possible there was tissue averaging affecting the results of the previous studies. The sensors in our study should be sampling from the affected compartment alone.

One limitation of this study and previous studies (16, 17) was the model chosen to represent ALCS. The infusion of 5% albumin was used to mimic effusive conditions of trauma as well as provide a means to increase compartment pressure in a controlled fashion. The model does not take into account the inflammatory response seen with ALCS, and in the trauma group,

may not represent the same inflammatory and vascular response as well as soft tissue trauma seen in ALCS. With potentially different underlying pathology, the fasciotomy may have different effect in ALCS compared to this model.

In both acute trauma and control groups a positive correlation was seen between tissue oxygenation as measured by NIRS and with TIPP while TIPP was above 0 mm Hg. The fall of TIPP below this critical level of 0 mm Hg caused significant drop of detectable tissue oxygenation yet progressively lower TIPP beyond this was not related to progressively lower tissue oxygenation as measured by NIRS. Likewise as TIPP increased after fasciotomy, initial increase was not correlated with increasing tissue oxygenation until this critical level was surpassed at which time NIRS values and TIPP regained a positive correlation. These findings may help to define where the threshold for ischemia occurs with PP (0 mm Hg) which is consistent with early studies (18, 25). These findings support the theory of PP playing a critical role in the development of ALCS.

The current data confirms that NIRS monitoring can provide important real time diagnostic information on tissue oxygenation in the face of potential ALCS as well as feedback on treatment endpoint measures for fasciotomy. Furthermore, NIRS is responsive to perfusion changes as they occur prior to any permanent muscle damage.

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Figure Legends

Figure 1: Depiction of instrumentation for NIRS and direct pressure monitoring

A and C = Albumin infusion (5% human albumin)

B and D = Direct pressure transducer measurement of compartmental pressure

E = NIRS sensor

**Fasciotomy incisions are indicated by the red lines located (on the image) to the left and right of NIRS sensor (E). The incision to the left represents the craniolateral fasciotomy (fasciotomy 1) and the incision to the right represents the caudolateral fasciotomy (fasciotomy 2).

Figure 2: Tibial Intracompartmental Pressure (TICP) and NIRS reported over time for control group.

s: start of each period, e: end of each period

MAP = mean arterial blood pressure

SAP = systolic blood pressure

SAP+10 = systolic blood pressure + 10 mm Hg

fasc 1: caudolateral fasciotomy, fasc 2: craniolateral fasciotomy

Long dash from fasc 1 to fasc+5 represents data from pigs that did not have a second fasciotomy.

Figure 3: Tibial Intracompartmental Perfusion Pressure (TIPP) and NIRS reported over time for control group.

see Figure 2 key

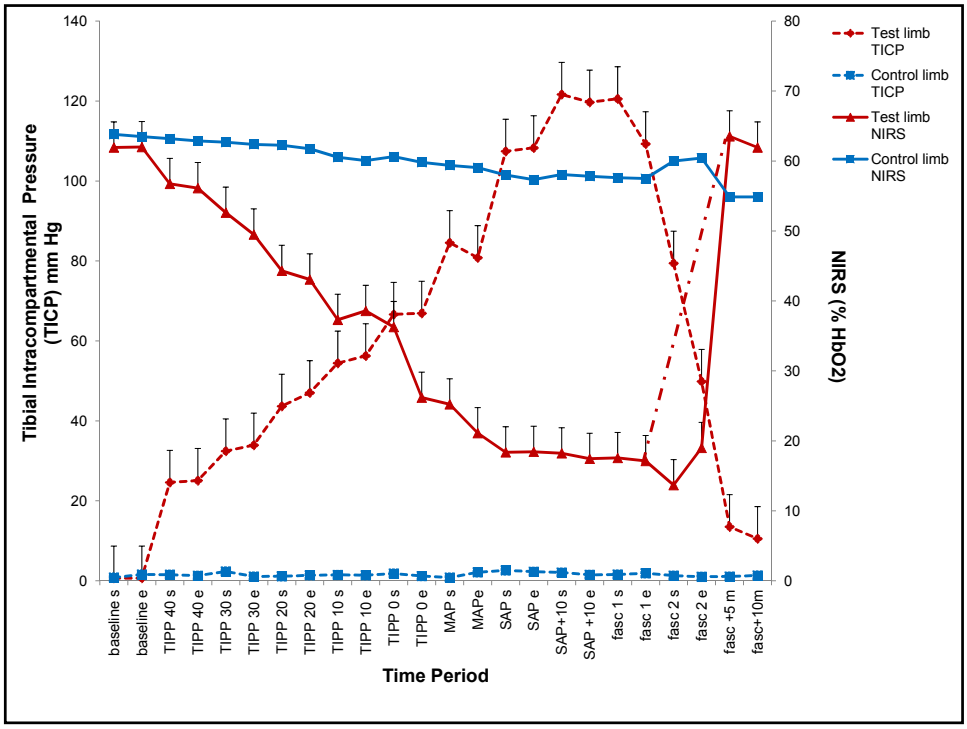
Figure 4: Tibial Intracompartmental Pressure (TICP) and NIRS reported over time for the acute trauma group.

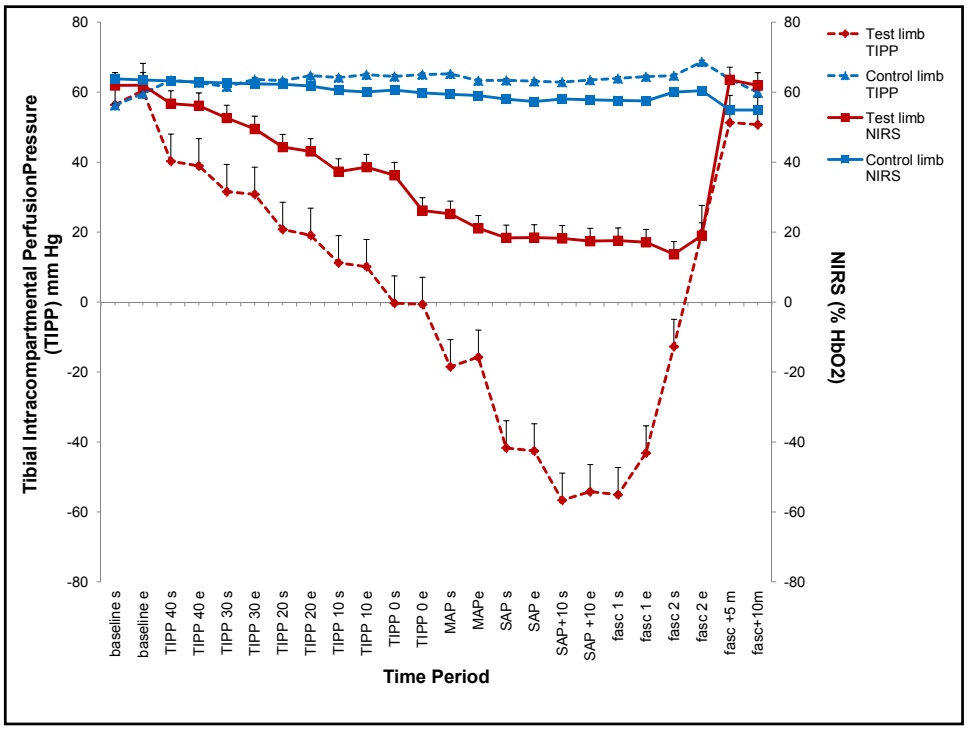
See Figure 2 key - PT equil: post trauma equilibration period

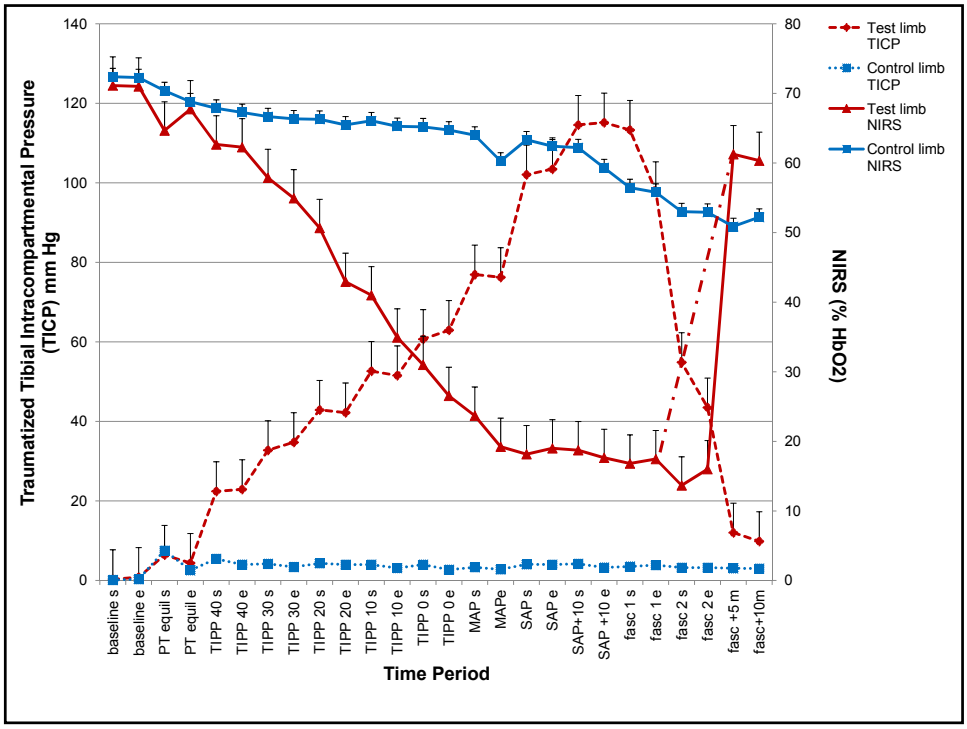
Figure 5: Tibial Intracompartmental Perfusion Pressure (TIPP) and NIRS reported over time for the acute trauma group.

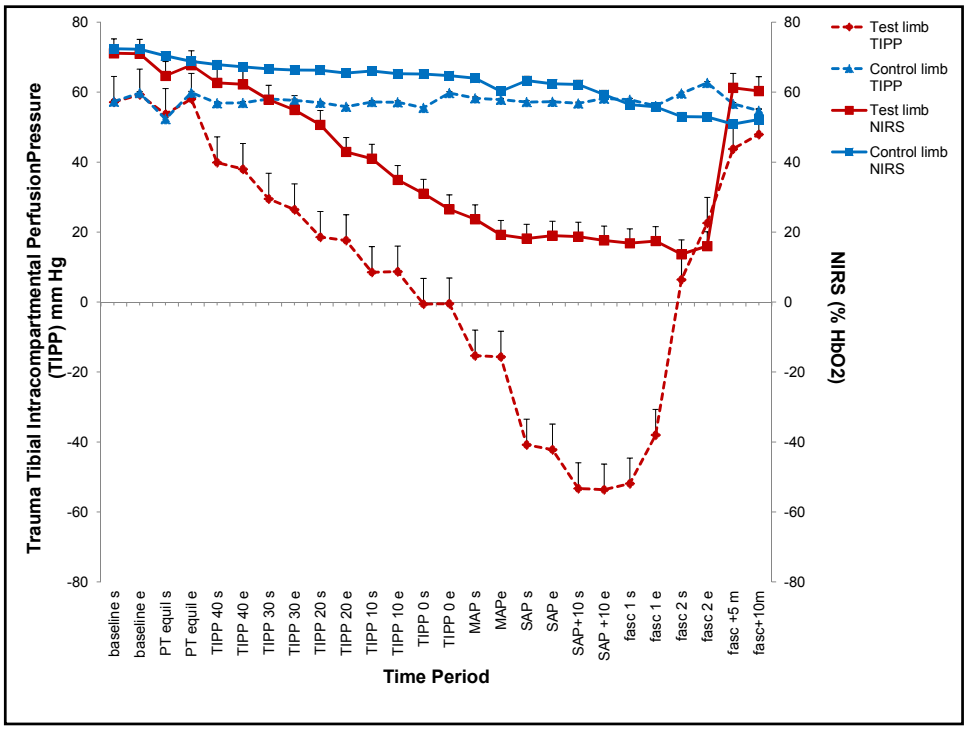
See Figure 4 key

Table 1: NIRS and perfusion pressures for the first 60 seconds after each fasciotomy for the two groups. This is data not included in figures 1-4.


Tibial Intracompartmental Pressure (TICP) mm Hg
NIRS (% HbO2)
Time Period
Test limb TICP
Control limb TICP
Test limb NIRS
Control limb NIRS
baseline s
baseline e
TIPP 40 s
TIPP 40 e
TIPP 30 s
TIPP 30 e
TIPP 20 s
TIPP 20 e
TIPP 10 s
TIPP 10 e
TIPP 0 s
TIPP 0 e
MAP s
MAPe
SAP s
SAP e
SAP+10 s
SAP +10 e
fasc 1 s
fasc 1 e
fasc 2 s
fasc 2 e
fasc +5 m
fasc+10m


Tibial Intracompartmental PerfusionPressure (TIPP) mm Hg
NIRS (% HbO2)
Time Period
Test limb TIPP
Control limb TIPP
Test limb NIRS
Control limb NIRS
baseline s
baseline e
TIPP 40 s
TIPP 40 e
TIPP 30 s
TIPP 30 e
TIPP 20 s
TIPP 20 e
TIPP 10 s
TIPP 10 e
TIPP 0 s
TIPP 0 e
MAP s
MAPe
SAP s
SAP e
SAP+10 s
SAP +10 e
fasc 1 s
fasc 1 e
fasc 2 s
fasc 2 e
fasc +5 m
fasc+10m


Traumatized Tibial Intracompartmental Pressure (TICP) mm Hg
NIRS (% HbO2)
Time Period
Test limb TICP
Control limb TICP
Test limb NIRS
Control limb NIRS
baseline s
baseline e
PT equil s
PT equil e
TIPP 40 s
TIPP 40 e
TIPP 30 s
TIPP 30 e
TIPP 20 s
TIPP 20 e
TIPP 10 s
TIPP 10 e
TIPP 0 s
TIPP 0 e
MAP s
MAPe
SAP s
SAP e
SAP+10 s
SAP +10 e
fasc 1 s
fasc 1 e
fasc 2 s
fasc 2 e
fasc +5 m
fasc+10m


Trauma Tibial Intracompartmental PerfusionPressure (TIPP) mm Hg
NIRS (% HbO2)
Time Period
Test limb TIPP
Control limb TIPP
Test limb NIRS
Control limb NIRS
baseline s
baseline e
PT equil s
PT equil e
TIPP 40 s
TIPP 40 e
TIPP 30 s
TIPP 30 e
TIPP 20 s
TIPP 20 e
TIPP 10 s
TIPP 10 e
TIPP 0 s
TIPP 0 e
MAP s
MAPe
SAP s
SAP e
SAP+10 s
SAP +10 e
fasc 1 s
fasc 1 e
fasc 2 s
fasc 2 e
fasc +5 m
fasc+10m

Control	Fasciotomy (1) n = 9		Fasciotomy (2) n = 7	
	NIRS Value	**Perfusion Pressure**	**NIRS Value**	**Perfusion Pressure**
Pre-first fasciotomy	23.8 ± 6.6	-49.0 ± 12.6	16.3 ± 0.5	-46.8 ± 26.7
30 seconds post 1st fasciotomy	24.5 ± 9.0	-16.4 ± 45.2	17.0 ± 0.0	-37.9 ± 32.2
60 seconds post 1st fasciotomy	40.2 ± 14.8	34.9 ± 18.8	16.0 ± 3.5	-26.6 ± 20.8
Post-2nd second fasciotomy				
30 seconds post 2nd fasciotomy	NA	NA	22.0 ± 11.7	33.5 ± 21.2
60 seconds post 2nd fasciotomy	NA	NA	35.3 ± 23.1	46.1 ± 13.3
Acute Trauma	**Fasciotomy (1) n = 4**		**Fasciotomy (2) n = 11**	
	NIRS Value	**Perfusion Pressure**	**NIRS Value**	**Perfusion Pressure**
Pre-first fasciotomy	24.7 ± 0.5	–52.1 ± 23.5	22.5 ± 4.1	-58.9 ± 22.8
30 seconds post 1st fasciotomy	35.0 ± 15.5	1.7 ± 22.6	23.5 ± 2.9	-36.4 ± 22.3
60 seconds post 1st fasciotomy	41.5 ±19.1	9.35 ± 35.4	21.7 ± 2.1	-5.86 ± 21.4
Post-2nd second fasciotomy				
30 seconds post 2nd fasciotomy	NA	NA	31.5 ± 12.7	33.6 ± 22.2
60 seconds post 2nd fasciotomy	NA	NA	43.1 ± 16.5	46.1 ± 13.3

Table 1: NIRS and perfusion pressures from the two groups during the fasciotomy portion of the experiment.